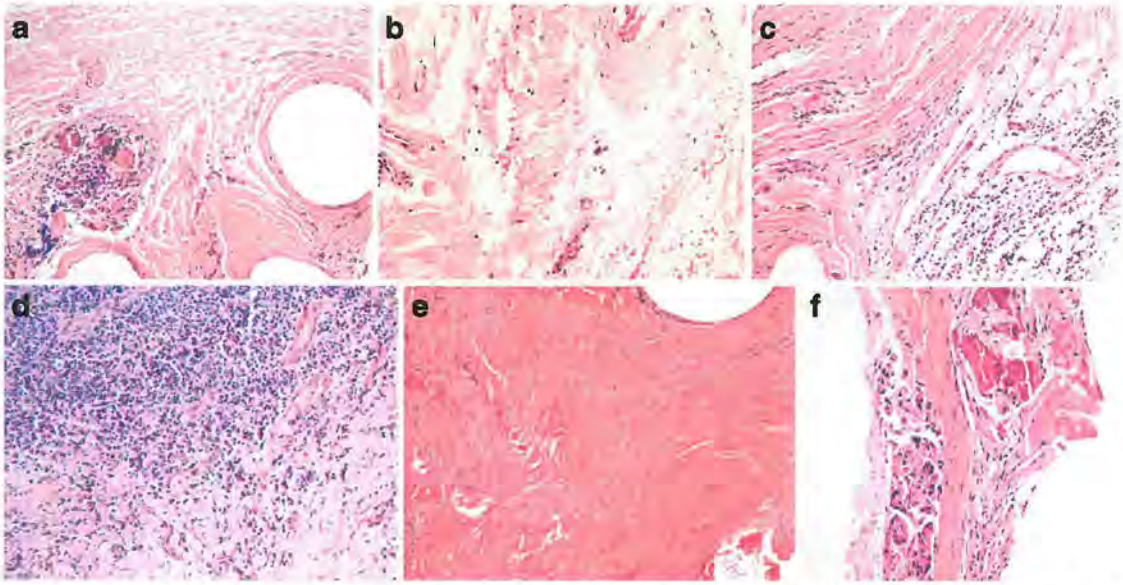

Fig. 1 Representative histological findings identified following mesh excision. **a** Grade 0 inflammation and grade 1 fibrosis: delicate loose fibrovascular connective tissue with scattered fibroblasts. Chronic inflammatory cells are absent. **b** Grade 1 inflammation: a sparse infiltrate of chronic inflammatory cells associated with mesh material and foreign body giant cell reaction. **c** Grade 2 inflammation and grade 2 fibrosis: chronic inflammatory cells are more numerous and are associated with foreign body giant cell reaction with extension into the adjacent connective tissue. The connective tissue is focally dense and fibrous. **d** Grade 3 inflammation: a markedly cellular chronic inflammatory infiltrate with lymphocytes and numerous plasma cells is associated with the foreign body giant cell reaction and extends into adjacent connective tissue. **e** Grade 3 fibrosis: dense fibrous connective tissue forming a fibrotic nodule. **f** Presence of giant cell reaction: numerous multinucleated giant cells with interspersed chronic inflammatory cells surround synthetic mesh material

fibrosis, and giant cell reaction. These results are consistent with some of the findings of Smith et al. [16]. In their study, 47 specimens of explanted vaginal mesh were reviewed histologically. Fibrosis was identified in 70.1 % of specimens. However, only 18.8 % of their specimens were noted to have a foreign body giant cell reaction and inflammation was reported in 10.4 % of the pathological specimens [16]. These results differed from ours, and this may be because the authors looked at all cases of explanted vaginal mesh for pelvic organ prolapse, while our study was designed to examine excised midurethral mesh only. Also, the grading system and criteria for inflammation that the authors used are not defined and may have differed from ours. Conversely, Wang et al. also looked at 20 pathological specimens of mesh explanted for failed anti-incontinence procedures and found them to mostly have moderate inflammation and foreign body reaction, which is consistent with our findings [19].

Subjects with voiding dysfunction but not pain or mesh exposure were found to have more inflammation than subjects who underwent mesh excision for pain and/or mesh erosion and those with both voiding dysfunction and pain/mesh exposure. This difference may be related to timing of mesh excision in patients with only voiding dysfunction. Voiding dysfunction is usually diagnosed in the immediate postoperative period, and if attributed to midurethral sling placement, mesh excision often occurs sooner in these patients than in those who present with pain and/or exposure. As a result, mesh specimens from these subjects would be expected to have higher degrees of inflammation compared to others as the healing process from the placement of the original implant would still be present. In our study population, only 72/130 (55 %) index surgery operative reports were available for review, and therefore we were unable to accurately report and compare time from index surgery to excision among the three groups in order to confirm this hypothesis.

Additionally, our findings could be a result of tissue remodeling/fibrosis that may occur following placement of a midurethral sling [17–19]. One could hypothesize that in the presence of an inflammatory state, the sling may retract and/or shrink therefore applying undue tension along its path, which in turn may lead to increased levels of voiding dysfunction.

Approximately 90 % of the pathological specimens in our study were found to have evidence of a giant cell reaction. This is consistent with what occurs after implantation of a biomedical device and is referred to as the "foreign body reaction" [15]. This is an immunologically mediated process that takes place at the cellular level and initially occurs during the first few weeks following implantation, but remains present at the device/host-tissue level for a lifetime depending on what kind of biomaterial is used [20]. Most of what we know about this process is a result of research that has looked at the host-tissue response with various biomaterials and/or mesh following implantation in both human and animal studies.

The strengths of our study include a large cohort of subjects. Additionally, all pathological specimens were rereviewed by a single pathologist who was blinded to the indication for mesh excision. Finally, our constructed histological grading system allowed for a systematic evaluation of individual specimens and allowed us to compare outcomes between the three groups. However, we do acknowledge that our grading system was specifically developed for this investigation and has not yet been validated by other facilities. The major limitation to this study is its retrospective design. We did not have access to all of the index surgery operative reports, and therefore we relied on subject recall as documented in the electronic medical record for some of our data. This limited our ability to analyze potential risk factors that may have led to increased levels of inflammation. These include the date of the index mesh placement, type of mesh utilized, and the surgical approach (i.e., transobturator or retropubic) that was performed. Additionally, not all subjects who underwent revision of their sling had pathological specimens for review. It is unknown if the findings at the time of the surgical procedure, i.e., signs of inflammation/infection or litigious indications, may have led to increased pathological submission. Lastly, the medical record was used to classify patients into their respective groups, which is also subject to information bias. Attempts were made to minimize these biases and measures were taken to ensure that strict criteria were used to classify subjects, and one researcher was responsible for all data collection.

Vaginally placed midurethral sling mesh that is excised for voiding dysfunction demonstrates elevated levels of inflammation compared to mesh that is excised for pain and/or exposure. Giant cell reaction also appears to be a ubiquitous finding in excised vaginal mesh, and the vaginal tissue response to midurethral mesh is histologically similar for fibrosis and giant cell reaction in all patients. We therefore can conclude that some histopathological indices may differ among specimens, and these differences may be related to the indication for midurethral mesh excision. While the clinical implications of this finding remain unclear, our results contribute to the limited data that exists on this subject, and future studies should aim at further investigating the host-tissue response as it relates to transvaginal mesh placement.

Conflicts of interest None.

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